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Severity of disease scoring systems and mortality after non-cardiac surgery

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Severity of disease scoring systems and mortality after non-cardiac surgery

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Abstract

Purpose: There are still high death rates related to surgeries mainly linked to postoperative period. Mortality prediction is one of the greatest challenges posed in intensive care and severity of disease scoring systems are the main tool available. The aim of this study was to evaluate predictors for postoperative mortality.

Methods: all adult patients who underwent non-cardiac surgery, admitted in a surgical intensive care unit (SICU) for longer than 12 hours between January 2006 and July 2013 were evaluated. Univariate analysis was carried using Mann-Whitney test, Chi-Square or Fischer's exact test. Multivariate analysis with logistic regression was performed with calculation of Odds Ratio (OR) with 95% confidence interval (CI).

Results: 4398 patients met the inclusion criteria. Mortality in SICU was 1.4%. Patients dying in the SICU had higher score in severity of disease scoring systems and length of stay. Multivariate analyses find 5 independent predictors of mortality in the SICU: APACHE II (OR 1.24, CI 1.17-1.30), emergent surgery (OR 4.10, CI 2.12-7.94), postoperative serum sodium (OR 1.06, CI 1.01-1.11), serum bicarbonate (OR 0.89, CI 0.82-0.96), and FiO2 (OR 14.31, CI 3.01-68.07).

Conclusion: independent predictors of SICU's mortality were APACHE II, emergent surgery, postoperative serum bicarbonate, serum sodium and FiO2.

Keywords: postoperative mortality, severity of disease scoring systems, APACHE II SAPS II, surgical intensive care unit, non-cardiac surgery

Abbreviations

ASA-PS: American Society of Anesthesiologists physical status; CI: confidence interval; GCS: glasgow coma scale; HR: heart rate; ICU: intensive care unit; LOS: length of stay; MAP: mean arterial pressure; OR: odds ratio; PACU: Post-Anesthesia Care Unit; RCRI: Revised Cardiac Risk Index; RR: respiratory rate; SAPS: Simplified Acute Physiology Score; SICU: surgical intensive care unit; SP: systolic pressure

Conflict of interest: none

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Introduction

It is estimated that every year 234.2 million people will be submitted to surgery worldwide (1).

According to the 2012 European Surgical Outcomes Study (EuSOS), 4% of patients died before hospital discharge (2) and postoperative one-year mortality was 5.5% (3). The majority of deaths occur in older patients who undergo major emergent surgery and who have severe coexisting diseases as well in those patients that develop complications (4-7).

There are several risk factors described for morbidity and mortality after surgery, which may be divided into three categories: patient-related, surgery-related and anesthesia-related. The risks of surgery and anesthesia are low for the majority of patients and evidence increasingly suggests that postoperative complications have a major impact on mortality (4, 5, 8). Developed countries have major morbidity due to postoperative complications (12 % in United States) (9). Thereof with aging and consequent increase of the patient's co-morbidities, as well as with increasing numbers of patients, there is an increase in postoperative morbidity and mortality (5, 10).

Half of the postoperative adverse events were identified as avoidable (11). Reducing rates of postoperative complications and their effective management may be one approach in reduce postoperative mortality (4, 5, 9). Immediate postoperative care allows a close monitoring and early intervention in order to prevent early postoperative complications and deaths. Seriously ill or at increased risk patients' may require more extensive monitoring in a surgical intensive care unit (SICU) which may contribute to a better outcome, decreasing morbidity and mortality. However there are few SICU's beds and high costs of their use (12, 13).

The study of outcome in critical care patients has been primarily focused on hospital survival and the resource utilization adjusted according to the severity of illness. Intensive care unit (ICU) case fatality rates strongly depend on the severity of illness of the individual in the patient population being analyzed (14).

To improve postoperative care, severity of disease scoring systems were used in order to predict the prognosis and estimate the morbidity and mortality of patients. Acting as outcome predictors they allow comparisons and the calculation of the expected mortality. Acute Physiology and Chronic Health Evaluation II (APACHE II) and Simplified Acute Physiology Score II (SAPS II) are two worldwide used severity of disease scoring systems (15-17).

The severity of scoring systems may be used to predict mortality with the calculation of the standardized mortality ratio (SMR), the ratio of observed to predicted mortality, which is used as an indicator of the quality of intensive care (18-20), although some authors argue that the SMR should not be used to measure the quality of care (21, 22). Several risk indices have been developed over the past years based on the relationship between comorbidities and perioperative morbidity and mortality. The Revised Cardiac Risk Index (RCRI) have become well known and although it isn't a severity of disease score has been used to predict an increased risk of cardiac complications after surgery being incorporated in guidelines for the study of preoperative risk factors (23, 24).
The aim of the present study was to evaluate the determinants of mortality using parameters included in severity of disease scoring systems in a cohort of critical surgical patients.

Methods

Data collection

The full study protocol was approved by the research ethics committee of the hospital. This prospective cohort study was carried out in the multidisciplinary Post-Anesthesia Care Unit (PACU) at the Hospital São João, an 1124-bed community teaching hospital in Porto, Portugal. Included in the PACU was a Surgical Intensive Care Unit (SICU) with five beds to which critically ill surgical patients are admitted and are closely monitored and treated.

All patients admitted at the SICU who underwent elective or emergent non-cardiac surgery between 1st January 2006 and 19th July 2013 were eligible for inclusion. Patients less than 18 years old, medical patients, re-admittance for the same medical reason during the studied period and SICU length of stay (LOS) lower than 12 hours were excluded.

The following variables were recorded at admission to the SICU: age, type of admission (elective or non-elective surgery) and mechanical ventilation.

For all patients we recorded the SICU LOS and the mortality in the SICU. Major cardiac event was defined as at least one of the following: acute myocardial infarction, acute pulmonary edema, primary cardiac arrest, ventricular fibrillation/other ventricular arrhythmias, complete heart block were assessed (25).

Organ insufficiency (considering presence of at least one organ failure defined by APACHE II) and renal insufficiency (considering creatinine > 2 mg/dL and/or oliguria of <500 ml / day) was also evaluated.

APACHE II and SAPS II were calculated. All variables and parameters included in APACHE II and SAPS II scores were evaluated separately (15, 17).

RCRI was also evaluated using criteria developed by Lee et al: high-risk surgery (intraperitoneal, intrathoracic, or suprainguinal vascular procedures), history of ischemic heart disease, history of congestive heart disease, preoperative insulin therapy, preoperative serum creatinine >2.0 mg/dL and history of cerebrovascular disease (23).

Statistical analysis

Descriptive analysis of variables was used to summarize data.

Kolmogorov-Smirnov Test for normality of the underlying population was performed.

The Mann-Whitney U test, the Chi-square and Fisher’s exact test were used in the univariate analyses to compare continuous variables and proportions, respectively.

To assess independent predictive factors of postoperative mortality, multivariate analysis were performed with multiple binary logistic regression. After applying the Bonferroni's correction for multiple comparisons, all the variables included in severity of disease scoring systems that had $p \leq 0.001$ in the univariate analyses were entered in a logistic multiple regression binary analysis with forward elimination method to examine covariate effects on mortality calculating an odds ratio (OR) and 95% confidence interval (CI)

The statistical software SPSS version 22.0 for Windows (SPSS, Chicago, IL) was used to analyze the data.

Results

During the study period there were 4561 admissions in the SICU and 4398 patients met the inclusion criteria. A total of 163 patients were excluded: 53 had a length of SICU stay lower than 12 hours, 42 were admitted more than once, 38 were younger than 18 years old and 30 were admitted for medical reasons. Sixty patients (1.4%) died in the SICU.

Table 1 display the characteristics of all patients enrolled in the study and the comparison between patients who survive and patients that have died during SICU stay. The median age was 65 years (IQR 54 -74 years) and 61% were male.

Thirteen percent of patients were admitted after non-elective surgery.

The median postoperative length of stay for all patients was 20 hours (IQR 16-42 hours).

One hundred and seven patients (2.4%) developed major cardiac event that include at least one of the following events: acute myocardial infarction (n=59), acute pulmonary edema (n=34), primary cardiac arrest (n=19), ventricular fibrillation/other ventricular arrhythmias (n=8) and complete heart block (n=4).

In univariate analyses patients that died were older (median 73 vs 65, $p<0.001$), were more likely to have been submitted to an emergent surgery (60% vs 12%, $p<0.001$), had more frequently mechanical ventilation on admission (83% vs 30%, $p<0.001$), renal insufficiency (35% vs 6%, $p<0.001$) and organ insufficiency (40% vs 15%, $p<0.001$). Patients that have died in SICU had lower hematocrit (median 29 vs 33, $p<0.001$), lower body temperature (median 34.0 vs 35.8, $p<0.001$), lower systolic pressure (median 77 vs 122, $p<0.001$), lower mean arterial pressure (median 54 vs 85, $p<0.001$), higher heart rate (median 112 vs 83, $p<0.001$), higher respiratory rate (median 16 vs 14, $p<0.001$), higher urea serum concentration (median 45 vs 30, $p<0.001$), higher serum creatinine (median 15.6 vs 8.2, $p<0.001$), higher total bilirubin (median 6 vs 4, $p<0.001$), higher FiO_2 (median 0.52 vs 0.40, $p<0.001$), lower PaO_2 (median 98 vs 100, $p=0.039$), higher $PaCO_2$ (median 42.7 vs 39.4, $p=0.001$), lower serum bicarbonate (median 19.4 vs 22.0, $p<0.001$), lower pH (median 7.28 vs 7.40, $p<0.001$), higher serum sodium (median 145 vs 140, $p<0.001$) and had more frequently a glasgow coma scale < 9 (8% vs 1%, $p<0.001$).

Table 2 displays severity of disease scores, length of stay and major cardiac events. Patients that died had higher scores of APACHE II (median 22 vs 8, $p<0.001$) and SAPS II (median 44 vs 18, $p<0.001$) and had more frequently major cardiac events

(28% vs 2%, $p<0.001$) and had a longer stay (median 46 vs 20, $p<0.001$) compared to survival group.

As displayed in table 3, patients not surviving had more frequently RCRI scores of more than 2 (18% versus 7%, $p=0.004$). These patients were submitted more frequently to a high-risk surgery (80% vs 54%, $p<0.001$).

In table 4 are the results of the multivariate analyses that showed that APACHE II (OR 1.24, 95% CI 1.17-1.30), type of admission as emergent (OR 4.10, 95% CI 2.12-7.94), FiO_2 (OR 14.31, 95%CI 3.01-68.07) and serum sodium (OR 1.06, 95% CI 1.01-1.11) are independent predictors of mortality while serum bicarbonate (for each 1 mmol/L increase) was associated with reduced risk of death (OR 0.89, 95% CI 0.82-0.96).

Discussion

In the present study, we assessed the mortality rate of a cohort of surgical critical patients after major surgery and studied predictors of mortality analyzing all variables included in the severity of score disease APACHE II and SAPS II.

The principal findings of this study were as follows: that the that mortality rate in the SICU was 1.4%; that patients not surviving after SICU admission had higher severity of disease scores according to SAPS II and APACHE II, they stayed longer in the SICU and had more frequently major cardiac events; almost all variables included in the severity of disease scoring systems were different in the group of patients not surviving in SICU. When adjusted for each other and maintaining severity of disease scores in the equation only APACHE II, emergent surgery type of admission, inspired fraction of oxygen and serum sodium were considered independent factors for mortality while a higher serum bicarbonate was associated with a reduction of mortality.

Early identification of patients at a higher risk of mortality may be important to promote treatment and orientation strategies that may preclude case fatalities (4, 6). Severity of disease scoring systems may allow us to estimate mortality risk in surgical critical patients (15-17) and identifying a group of patients at increased risk of dying.

Previous studies have been focused on identifying predictors of postoperative mortality and morbidity evaluating and quantifying comorbidities, perioperative factors and the presence of postoperative complications (3-6, 25-33), but no studies have attempted to identify predictors within routine physiological and analytical postoperative parameters included in severity of disease scoring systems.

Type of surgery is a variable that has been studied and clearly found to be related to mortality (6, 7, 10, 30, 34) and our results indicate as well that emergent surgery patients had a higher mortality rate. It seems that patients undergoing non-elective surgeries are likely to have a worse prognosis since they were more severely ill with a higher grade of comorbidities with a higher probability of having a less functional reserve. Because of that these patients may be submitted to more complex surgeries and they usually require a careful intraoperative care (10, 35). In our study non-elective emergent surgery was considered an independent predictor of mortality, increasing the probability of dying in the SICU almost 4 times.

In multivariate analysis FIO2 was another independent predictor of mortality. Higher FiO2 is frequently required in patients with impaired tissue oxygenation trying to avoid the harmful effects of hypoxia. In fact it is well documented that the PaO2/FiO2 ratio is associated with mortality (36, 37). In our study we did not studied this equation fraction but the isolated FiO2 parameter may be considered as a relevant surrogate indicator of that fraction. In a previous study higher FiO2 remained an independent predictor of mortality even after adjustment for PaO2/FiO2 ratio (38), suggesting poor prognosis not only because these patients are more severely ill with impaired tissue oxygenation, but also because of hyperoxia and ventilation side-effects (38-40).

Others have found serum sodium to be a reliable risk factor for mortality (41-45) and it is not surprisingly that in this study serum sodium was considered an independent risk factor for mortality. Hypernatremia is a common complication in critically ill patients such they may be unconscious, intubated or sedated and may invariably denotes hyperosmolar state and transiently intracellular dehydration (46).

The multivariate analysis of independent variables showed that higher serum bicarbonate was associated with a reduction of mortality for each mmol increment having a positive impact on survival. This result may indicate that a lower serum bicarbonate levels was associated with metabolic acidosis and consequently with case fatalities that has been shown by others (47-50). Although the deleterious impact of lower serum bicarbonate is well known, both lower and higher serum bicarbonates may be associated with increased all-cause mortality as a result of the well documented consequences of acid-base abnormalities that have been associated with adverse outcomes such as increased mortality (51). However, a recent retrospective analysis shows that acidosis itself had no relation with poor outcome which was more dependent on severe conditions associated with acidosis (52).

Age have also been found to have a clear association with postoperative mortality (3, 6, 53) and that is why is not surprisingly that in our study patients that died in the SICU were older.

In order to stratify the preoperative risk of patients we relied on the RCRI. Patients that died had more frequently a score greater or equal than 2 but only high-risk surgery were considered a risk factor for mortality and it is interesting that comorbidities included in RCRI did not appear to be related to mortality. Perhaps in this particular group of major surgery patients the burden of surgery was more relevant than comorbidities.

Patients with prolonged SICU LOS had higher mortality as LOS is needed in patients who develop postoperative complications and those who were more severely ill (7, 25-27).

Data suggest that complication rate varies between 7% and 11% (54). The occurrence of postoperative cardiac events is not uncommon, occurring in 2.4% in this study. Furthermore mortality group had significantly more major cardiac events, corroborating previous studies showing that patients with postoperative major cardiac events had higher mortality (25, 26). Indeed previous studies show that cardiovascular complications are the leading causes of morbidity in older patients (10) and may be associated with 42% of deaths (34).

We know that many other complications are related to increased risk of mortality (4, 9, 55) and that many of the surviving patients suffer major complications with a variety of morbidity and the consequent reduction of the health and quality of life (26, 56).

Study limitations

Besides the limitations inherent to a retrospective cohort study, others are present on the design of this study. Preoperative risk assessment is roughly based on three broad but connected categories including several risk factors: surgery-related, patient-related or dependent on patient's functional status. Not knowing the pre-existing conditions of patients beyond the comorbidities present in the Revised Cardiac Risk Index probably may also limit the value of conclusions, because comorbidities others than those we have studied may be closely related and may have a clear influence on physiological parameters included in the severity of disease scoring systems (for example chronic obstructive pulmonary disease and PaO2). The lack of an American Society of Anesthesiologists physical status (ASA-PS) for our sample population was also questionable. Risk prediction models for intraoperative and postoperative mortality have included the ASA-PS classification as one strong predictor (24, 57-59).

Other limitation of the study is the missing data about in-hospital mortality what may be viewed as an important limitation since severity of disease scores and its standard mortality rates are related to hospital mortality not to ICU mortality.

Furthermore, neither intraoperative hemodynamic parameters nor other postoperative complications beyond organ insufficiency, renal insufficiency and major cardiac events were evaluated in our study and this may be viewed as a limitation that certainly had influenced outcome and mortality.

Conclusions

In conclusion postoperative mortality during SICU stay was 1.4%. Fatalities cases had significantly higher scores in severity of disease scoring systems as well as had a longer SICU stay and more major cardiac events. We have identified independent risk factors for mortality: APACHE II, FiO2, serum sodium, type of admission while higher serum bicarbonate was associated with a reduction of mortality.

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Tables

Table 1: Univariate analysis of mortality predictors in SICU – patients' characteristics

Variables	**Total N=4398**	**Survival group N=4338**	**Mortality group N=60**	**p value**
Gender, n (%)				
Male	2681 (61.0)	2642 (60.9)	39 (65.0)	0.518 [a)]
Female	1717 (39.0)	1696 (39.1)	21 (35.0)	
Age, median (IQR)	65.0 (54.0-74.0)	65.0 (53.0-74.0)	72.5 (59.5-79.8)	<0.001 [b)]
Type of admission, n (%)				
Elective surgery	3827 (87.0)	3803 (87.7)	24 (40.0)	<0.001 [a)]
Non-elective surgery	571 (13.0)	535 (12.3)	36 (60.0)	
Mechanical ventilation on admission, n (%)	1341 (30.5)	1291 (29.8)	50 (83.3)	<0.001 [a)]
Renal insufficiency, n (%)	285 (6.5)	264 (6.1)	21 (35.0)	<0.001 [f)]
Organ insufficiency, n (%)	682 (15.5)	658 (15.2)	24 (40.0)	<0.001 [a)]
Hematocrit, median (IQR)	33.0 (29.8-36.3)	33.0 (29.9-36.4)	28.8 (22.9-33.0)	<0.001 [b)]
Body temperature, median (IQR)	35.4 (34.6-36.0)	35.8 (34.6-36.0)	34.0 (33.0-35.3)	<0.001 [b)]
Systolic pressure, median (IQR)	122.0 (102.0-144.0)	122.0 (102.0-144.0)	76.5 (66.0-88.8)	<0.001 [b)]
Mean arterial pressure, median (IQR)	85.0 (71.0-96.0)	85.0 (71.0-96.0)	53.0 (47.3-63.0)	<0.001 [b)]
Heart rate, median (IQR)	83 (69-98)	83 (68-98)	112 (88-133)	<0.001 [b)]
Respiratory rate, median (IQR)	14 (12-16)	14 (12-16)	16 (14-16)	<0.001 [b)]
Serum urea, median (IQR)	30.0 (20.0-40.0)	30.0 (20.0-40.0)	45.0 (23.5-70.0)	0.001 [b)]
Serum creatinine, median (IQR)	8.3 (6.5-11.0)	8.2 (6.5-11.0)	15.6 (9.0-25.3)	<0.001 [b)]
Total bilirrubin, median (IQR)	4.0 (1.0-7.0)	4.0 (1.0-7.0)	6.0 (4.0-10.8)	<0.001 [b)]
FiO2, median (IQR)	0.40 (0.35-0.40)	0.40 (0.34-0.40)	0.52 (0.40-1.00)	<0.001 [b)]
PaO2, median (IQR)	100.0 (100.0-110.0)	100.0 (100.0-110.0)	98.0 (75.5-138.6)	0.039 [b)]
PaCO2, median (IQR)	39.5 (35.0-45.0)	39.4 (35.0-45.0)	42.7 (36.0-54.0)	0.001 [b)]
Serum bicarbonate, median (IQR)	22.0 (21.0-24.0)	22.0 (21.0-24.0)	19.4 (17.0-22.0)	<0.001 [b)]
pH, median (IQR)	7.40 (7.35-7.40)	7.40 (7.35-7.40)	7.28 (7.17-7.35)	<0.001 [b)]
Serum potassium, median (IQR)	3.80 (3.40-4.10)	3.80 (3.40-4.10)	3.90 (3.13-4.45)	0.806 [b)]
Serum sodium, median (IQR)	140 (137-142)	140 (137-142)	145 (140-152)	<0.001 [b)]
Leucocytes count, median (IQR)	11.0 (8.0-14.0)	11.0 (8.0-11.0)	9.5 (4.0-19.0)	0.230 [b)]

Glasgow coma scale (<9), n (%)	54 (1.2)	46 (1.1)	8 (13.3)	<0.001[f)]

APACHE II: Acute Physiology and Chronic Health Evaluation; IQR: Interquartile range (P25-P75);

SAPS II: Simplified Acute Physiology Score; SICU: Surgical Intensive Care Unit

[a)]Chi-Square test

[b)] Mann-Whitney test

[f)] p value with Fisher's Exact Test

Table 2: Univariate analysis of mortality predictors in SICU - severity of disease scores, length of stay and major cardiac event.

Variables	**Total N=4398**	**Survival group N=4338**	**Mortality group N=60**	**p value**
APACHE II, median (IQR)	8.0 (6.0-12.0)	8.0 (6.0-12.0)	22.0 (19.0-26.0)	<0.001 [b)]
SAPS II, median (IQR)	18.0 (13.3-26.7)	18.0 (13.3-25.0)	43.7 (37.8-57.8)	<0.001 [b)]
SICU LOS(hours), median (IQR)	20.0 (16.0-42.0)	20.0 (16.0-41.0)	46.0 (19.5-82.8)	<0.001[b)]
Major cardiac event , n (%)	107 (2.4)	90 (2.1)	17 (28.3)	<0.001[f)]

APACHE II: Acute Physiology and Chronic Health Evaluation; IQR: Interquartile range (P25-P75); LOS: length of stay; SAPS II: Simplified Acute Physiology Score; SICU: Surgical Intensive Care Unit

[b)] Mann-Whitney test

[f)] p value with Fisher's Exact Test

Table 3: Univariate analysis of mortality predictors in SICU - Criteria developed by Lee et al

Variables	**Total N=4398**	**Survival group N=4338**	**Mortality group N=60**	**p value**
High-risk surgery, n (%)	2382 (54.2)	2334 (53.8)	48 (80.0)	<0.001 [a)]
History of ischemic heart disease, n (%)	617 (14.0)	607 (14.0)	10 (16.7)	0.554 [a)]
History of congestive heart disease, n (%)	691 (15.7)	673 (15.5)	18 (30.0)	0.002 [a)]
Preoperative insulin therapy, n (%)	215 (4.9)	213 (4.9)	2 (3.3)	1[f)]
Preoperative serum creatinine >2.0 mg/dL, n (%)	281 (6.4)	272 (6.3)	9 (15.0)	0.013[f)]
History of cerebrovascular disease, n (%)	559 (12.7)	548 (12.6)	11 (18.3)	0.188 [a)]
RCRI ≥2, n (%)	328 (7.5)	317 (7.3)	11 (18.3)	0.004[f)]

RCRI: Revised Cardiac Risk Index; SICU: Surgical Intensive Care Unit

[a)]Chi-Square test

[f)] p value with Fisher's Exact Test

Table 4: Multiple logistic regression analysis for independent predictors of mortality in SICU

Variables	**OR [a] (95% IC)**	**p [b] value**
APACHE II	1.25 (1.18- 1.31)	<0.001
Type of admission	3.88 (2.02- 7.46)	<0.001
FIO2	21.25 (4.75- 95.16)	<0.001
Serum bicarbonate	0.88 (0.82- 0.95)	0.001
Serum sodium	1.06 (1.01- 1.11)	0.01

APACHE II: Acute Physiology and Chronic Health Evaluation; CI: confidence interval; OR: odds ratio; SICU: Surgical Intensive Care Unit;

[a] Adjusted for age, mechanical ventilation on admission, renal insufficiency, organ insufficiency, hematocrit, body temperature, systolic pressure, mean arterial pressure, heart rate, respiratory rate, serum urea, serum creatinine, total bilirubin, FiO2, PaCO2, serum bicarbonate, pH, serum sodium, glasgow coma scale and SAPS II

[b] A logistic regression analysis with inclusion severity of disease scoring systems' variables with $p \leq 0.001$ was used.

Com toda a sinceridade agradeço ao meu orientador, Prof. Doutor Fernando Abelha, pela oportunidade de realizar este trabalho e por todo o apoio e aconselhamento durante o seu desenvolvimento. Agradeço ainda toda a compreensão e disponibilidade. Obrigada!

JOURNAL OF CRITICAL CARE

Improving Patient Care by Integrating Critical Care Systems Knowledge into Practice Behavior

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Centro Hospitalar de S. João, 15 de Dezembro de 2014

O Secretário da Comissão de Ética para a Saúde

Pedro Brito